REMARKS/ARGUMENTS

I. STATUS OF THE CLAIMS

With entry of this amendment, claims 2, 5-6, and 15-22 are canceled and claim 25 is newly added. Claims 1, 3, 4, 7-14, 23-25 are pending, and claims 1, 3, 4, 7-9, 10, 11, and 14 are currently amended. Support for the amendments can be found throughout the specification, drawings, and claims as originally filed. In particular, claims 1 and 7 are amended to replace the phrase "non-human animal" with "non-human mammal." Support for this amendment can be found for example at page 9, lines 23-28 of the specification. Claim 1 is further amended to introduce the phrase "without affecting cellular function." Support for this amendment can be found at page 15, lines 13-16 of the specification. Claim 1 is also amended to clarify that "the vector comprises the exogenous gene inserted between a first and a second ZO-1 gene fragment, wherein the first and second ZO-1 gene fragments are in the same order as that of the native ZO-1 gene." Support for this amendment can be found for example, Figures 1 and 3, wherein the order of the ZO-1 gene fragments is readily apparent and the same as that of the native ZO-1 gene.

The amendment to claim 3 merely replaces the phrase "the partial region of the ZO-1 gene" with "one of said first and second ZO-1 gene fragments" in accordance with the amendment to claim 1. Claim 4 is also amended in accordance with claim 1 to appropriately include the phrases "said first ZO-1 gene fragment comprises" and "said second ZO-1 fragment comprises." Claim 10 is amended for clarification purposes to delete the phrase "vector comprises a structure in which an."

Claim 25, directed to a linearized targeting vector comprising the in the 5' to 3' direction a first ZO-1 gene fragment, an exogenous gene, and a second ZO-1 gene fragment. Support for claim 25 can be found for example in Example 2, page 13, line 32, and in Figures 1 and 3 as originally filed. No new matter is added.

II. REJECTIONS UNDER 35 U.S.C. §112, FIRST PARAGRAPH

Claims 1-4, 7-14, 23 and 24 stand rejected under 35 U.S.C. §112, first paragraph as failing to comply with the written description requirement. The Examiner alleges that

although the specification only discloses a single species of ZO-1 gene (*i.e.* mouse ZO-1 gene) the claims when given their broadest reasonable interpretation, encompass a vector comprising a ZO-1 gene from any species of any non-human animal. As acknowledged by the Examiner, ZO-1 gene sequences from five other species were known in the art at the time of filing the instant application. The Examiner nevertheless alleges that the instant disclosure fails to demonstrate possession of the broad genus of ZO-1 genes isolated from any species, and concludes that the specification fails to provide adequate written description for the genus of ZO-1 genes encompassed by the claims. Applicants disagree.

In an effort to expedite the prosecution of the application, Applicants have amended claims 1 and 7 to replace the phrase "non-human animal" with "non-human mammal." In addition, Applicants submit a sequence alignment of the ZO-1 gene from various mammalian species including mouse, dog, rat and chimpanzee. *See,* **Exhibit A**. The sequence alignments clearly indicate that the genus of ZO-1 genes is not highly variable and unpredictable as alleged by the Examiner. Accordingly, the murine ZO-1 sequence, disclosed in the specification as SEQ ID NO:1, along with the other ZO-1 sequences known in the art at the time of filing the instant application constitute a representative number of species sufficient to demonstrate possession of the entire genus of ZO-1 sequences from non-human mammals, as presently claimed.

Furthermore, it is submitted that the rejection of claim 14 as failing to meet the written description requirement is improper. Specifically, claim 14 recites that the non-human mammal is a mouse. As acknowledged by the Examiner, the specification discloses the mouse ZO-1 gene as shown in SEQ ID NO 1.

In light of the arguments as presented above, and the claims as presently amended, Applicants request that the Examiner withdraw the rejections.

III. REJECTION UNDER 35 U.S.C. §102(b)

Claims 1-3, 8-12, 14, and 23 stand rejected under 35 U.S.C. §102(b) as allegedly anticipated by Itoh *et al.* (*J. Cell Biol.* (1993) 121:491-502). The Examiner alleges that Itoh *et al.* discloses a pBluescript SK(-) vector comprising (a) the entire mouse ZO-1 cDNA, including exon II, and (b) two heterologous genes (lacZ and bla(Ap^R)) each of which comprises a promoter

capable of transcribing the exogenous gene and may be considered "a marker gene expression cassette." The Examiner further alleges that because the vector in Itoh *et al.* is circular, each gene in the vector disclosed by Itoh *et al.* can be considered to be upstream and/or downstream of every other gene in the vector. *See*, page 7, lines 6-9 of the Office Action. The Examiner thus alleges that Itoh *et al.* anticipates the invention as recited in claims 1-3, 8-12, 14 and 23 prior to entry of this amendment. Applicants disagree.

In an effort to expedite prosecution of the application, independent claim 1 is currently amended to clarify that the vector comprises the exogenous gene between a first and a second fragment of the ZO-1 gene, wherein the first and second ZO-1 gene fragments are in the same order as in the native gene.

The vector disclosed in Itoh *et al.* is a circular cloning vector in which the heterologous genes are construed by the Examiner to be both upstream and downstream of the ZO-1 gene. The targeting vector of the instant invention as presently claimed places the exogenous gene within the ZO-1 gene such that the exogenous gene is inserted between a first ZO-1 gene fragment and a second ZO-1 gene fragment, with the additional limitation that the first and second ZO-1 gene fragments are in the same order as in the native ZO-1 gene. Itoh *et al.* does not disclose such an orientation.

Because Itoh *et al.* does not disclose a vector wherein an exogenous gene is inserted between a first and a second ZO-1 gene fragment where the first and second ZO-1 gene fragments are in the same order as in the native gene, Itoh *et al.* cannot anticipate the invention as presently claimed. Therefore, independent claim 1 is patentable and not anticipated by Itoh *et al.*

Claims 2, 3, 8-12, 14 and 23 depend either directly or indirectly from independent claim 1 and include all of the limitations of independent claim 1. The arguments as presented above are also applicable to the dependent claims.

In view of the claims as amended, and the arguments as presented above, Applicants request that the Examiner withdraw the rejection.

Claim 25 is not anticipated by Itoh *et al*

As acknowledged by the Examiner, the vector in Itoh *et al.* is circular and is construed by the Examiner to be read such that each gene is both upstream and downstream of every other gene on the vector as discussed above. Claim 25 is directed to a linear targeting vector wherein the exogenous gene is between a first and a second ZO-1 gene fragment. The linear vector only allows for a single orientation such that each gene on the vector is either be upstream or downstream from every other gene on the vector, not both. Because Itoh *et al.* does not disclose a linearized vector, as presently recited in independent claim 25, Itoh *et al.* cannot anticipate claim 25. Therefore, claim 25 is patentable and not anticipated by Itoh *et al.*

IV. REJECTION UNDER 35 U.S.C. §103(a)

A. Claims 1 and 7 are patentable and not obvious over Flemming *et al.* (*Devel.* (1991) 113:295-304) in view of LeMouellic *et al.* (*Proc. Natl. Acad. Sci.* (1990) 87:4712-4716) and Itoh *et al.*

Claims 1 and 7 stand rejected under 35 U.S.C. §103(b) as allegedly being obvious and unpatentable over Flemming *et al.* in view of LeMouellic *et al.* and Itoh *et al.* The Examiner cites Flemming *et al.* as allegedly teaching a method of investigating ZO-1 expression in embryos using an antibody against the ZO-1 protein. The Examiner cites LeMouellic *et al.* as allegedly disclosing a method of following tissue expression of a gene by inserting a marker gene into a targeting vector and integrating the targeting vector into an endogenous gene such that the endogenous gene is inactivated and the marker gene is placed under the control of the endogenous promoter. The Examiner cites Itoh, *et al.* as allegedly teaching the sequence of the mouse ZO-1 gene. In supporting the *prima facie* case, the Examiner concludes that it would have been obvious to substitute the reporter gene assay of LeMouellic *et al.* for the immunohistochemistry method of Flemming *et al.* using the mouse ZO-1 gene disclosed by Itoh *et al.* to arrive at a targeting vector as claimed in the instant invention. Applicants disagree.

As discussed above, Itoh *et al.* does not teach or suggest a targeting vector having the orientation as presently recited in claim 1, wherein the exogenous gene is inserted between a first and a second ZO-1 gene fragments, and wherein the first and second ZO-1 gene fragments

are in the same order as in the native gene as presently claimed. Furthermore, neither Flemming *et al.* nor LeMouellic *et al.* cure this defect. Therefore, the combination of the cited references do not teach or suggest all of the elements of independent claim 1 as presently recited, and therefore the rejection is improper.

Assuming arguendo, that the combined teachings of the cited references did support a *prima facie* case of obviousness, which the applicants contest, the present invention provides for surprising results that are not taught nor suggested by the prior art.

As disclosed in the instant specification at page 1, lines 20-21, "frequency of homologous recombination is generally very low *i.e.*, only about 0.1 to 1% in cells that have been introduced with the exogenous gene." Indeed, LeMouellic *et al.* confirms this teaching that "homologous recombination can be a rather rare event." *See*, Lemouellic *et al.* page 4713, right column lines 14-15. The present inventors have surprisingly discovered for the first time that high efficiency gene targeting can be achieved by making the ZO-1 gene a target site for introducing exogenous genes. The gene targeting vector of the instant invention enables homologous recombination with a 90% or higher probability without affecting cellular function. *See*, page 2, lines 12-13 of the specification. The targeting vector of the instant invention overcomes drawbacks associated with the conventional methods of generating transgenic mice, in particular the low frequency of homologous recombination events and the difficulty of expressing the exogenous gene without affecting cellular function.

Even if a skilled artisan were motivated to investigate the function of a ZO-1 gene based on the teachings of Flemming *et al.* to produce a targeting vector comprising the mouse ZO-1 gene sequence disclosed in Itoh *et al.* using the method of LeMouellic *et al.* in view of the technical knowledge at the time of filing, the skilled artisan would not expect the probability of homologous recombination to be at least 90% as achieved by the targeting vectors of the instant invention.

Independent claim 1 is patentable and not obvious over the cited references because the combination of the cited references do not teach nor suggest all of the limitations of independent claim 1 as presently recited, nor do the cited references teach or suggest the

surprising discovery that homologous recombination with a 90% or higher probability can be achieved using the targeting vectors of the instant invention.

Claim 7 depends from independent claim 1, and includes all of the limitations of independent claim 1. Therefore, the arguments as presented above are also applicable to dependent claim 7.

In view of the claims as presently amended, and the arguments as presented above, Applicants request that the Examiner withdraw the rejection.

B. Claims 1-3, 7-12, 14 and 23 are patentable and not obvious over Capecchi *et al.* (*Scientific American* (1994) 270:34-41) and Itoh *et al.*

Claims 1-3, 7-12, 14 and 23 stand rejected under 35 U.S.C. §103(a) as allegedly being anticipated by Capecchi and Itoh. The Examiner cites Capecchi *et al.* as teaching the generation of a mouse whose genome comprises a disruption in the HoxA-3 gene using targeting vectors comprising a first and a second polynucleotide sequences homologous to the target gene (HoxA-3) and a selectable marker. The Examiner alleges that Capecchi *et al.* merely differs from the instant invention in that it does not disrupt the ZO-1 gene. The Examiner relies on Itoh *et al.* as curing this defect. The Examiner concludes that it would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize the method of Capecchi *et al.* to disrupt the ZO-1 gene as disclosed by Itoh *et al.* to arrive at the Applicant's invention. Applicants disagree.

As Capecchi *et al.* acknowledges at page 38 bottom of right column to page 39 left col., line 5, it was recognized in the art at the time the present application was filed that targeted replacement occurs only in a small fraction of treated cells. Therefore, even if the skilled artisan were motivated to combine the teachings of Capecchi *et al.* to the ZO-1 gene as disclosed by Itoh *et al.*, the skilled artisan would not expect to produce a targeting vector as presently recited in independent claim 1 that displays the surprising results of enabling homologous recombination with a 90% or higher probability without affecting cellular function as discussed above in sections III and IV(A).

Claims 2-3, 7-12, 14 and 23 depend either directly or indirectly from independent claim 1, and include all of the limitations of independent claim 1. Therefore, the arguments as presented above with regard to independent claim 1 are also applicable to the dependent claims.

In light of the claims as presently recited and the arguments presented herein, Applicants request that the Examiner withdraw the rejection.

C. Claims 13 and 24 are patentable and not obvious over Capecchi *et al.*, in view of Itoh *et al.*, and in further view of Blake *et al.* (*Biotechniques* (1997) 23:690-695).

Claims 13 and 24 stand rejected under 35 U.S.C. §103(a) as allegedly being obvious and unpatentable over Capecchi *et al.* in view of Itoh *et al.* in further view of Blake *et al.* The Examiner alleges that it would have been obvious to one of ordinary skill in the art to substitute the neomycin resistance gene utilized by Capecchi *et al.* with the β-geo marker gene disclosed by Blake *et al.* because they are equivalent alternatives known at the time of the invention. Applicants disagree.

Claims 13 and 24 depend either directly or indirectly from independent claim 1 and include all of the limitations of independent claim 1. As discussed above, Capecchi *et al.* and Itoh *et al.* do not render independent claim 1 obvious or unpatentable, and these arguments are also applicable to dependent claims 13 and 24. Blake *et al.* does not cure the defects of Capecchi *et al.* and Itoh *et al.* as discussed above. Therefore the combination of the references do not render dependent claims 13 and 24 obvious or unpatentable over the cited references.

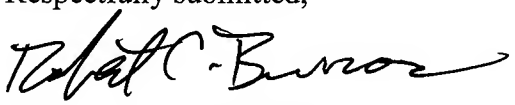
In light of the claims as presently amended, and the arguments as presented herein, Applicants request that the Examiner withdraw the rejection.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,



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Attachments
RCB:rcb
61482565 v1

EXHIBIT A

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options = -align -type=dna -matrix=blosum -gapdist=8 -maxdiv=40 -outorder=input -gapopen=15 -gapext=6.66 -pw

 CLUSTAL W (1.83) Multiple Sequence Alignments


Sequence type explicitly set to DNA
Sequence format is Pearson
Sequence 1: mouseZO-1          7046 bp
Sequence 2: ratZO-1            6614 bp
Sequence 3: dogZO-1            6805 bp
Sequence 4: chimpanzeeZO-1     7253 bp
Start of Pairwise alignments
Aligning...
Sequences (1:2) Aligned. Score:  94
Sequences (1:3) Aligned. Score:  85
Sequences (1:4) Aligned. Score:  82
Sequences (2:3) Aligned. Score:  87
Sequences (2:4) Aligned. Score:  88
Sequences (3:4) Aligned. Score:  89
Start of Multiple Alignment
There are 3 groups
Aligning...
Group 1: Sequences:   2      Score:118975
Group 2: Sequences:   2      Score:120536
Group 3: Sequences:   4      Score:113507
Alignment Score 242177


query.aln
CLUSTAL W (1.83) multiple sequence alignment

mouseZO-1          CGCCTGAGTTGCCCGCGACGGCTCTGCCCGCCGACGGCACGTCTCTCGGCGGCCGCGCGT
ratZO-1            ------------------------------------------------------------
dogZO-1            ------------------------------------------------------------
chimpanzeeZO-1     ------------------------------------------------------------

mouseZO-1          TCCGGGGAAGTTACGTGCGGGAGCAGGCTTTGGAGGAGACGCCCGAGGGTGTAGGGGACA
ratZO-1            ------------------------------------------------------------
dogZO-1            ------------------------------------------------------------
chimpanzeeZO-1     ------------------------------------------------------------

mouseZO-1          GCCGGAGGCCCGGGTACTGCGGAGCGGCGAGCCGGCGGAGGGCGGCGGAGGCCGAGCAGG
ratZO-1            ------------------------------------------------------------
dogZO-1            ------------------------------------------------------------
chimpanzeeZO-1     ------------------------------------------------------------

mouseZO-1          CGGCCGGGTGTGCCCCGCGGAGAAGCCCGGGCGGGGCGGACGCTTCCCGGACTTTTGTCC
ratZO-1            ------------------------------------------------------------
dogZO-1            ------------------------------------------------------------
chimpanzeeZO-1     -CCGCGAGCGAGCGGGACAAGATGAGTACCAGAATACCTGACGGTGCTGCAGATGGCCAT

mouseZO-1          CACTTGAATCCCCTCCCCGTGGGCCGGGCCTTTCCGGCCTCCCCCGCCCCTGCCCCGCTC
ratZO-1            ------------------------------------------------------------
dogZO-1            ------------------------------------------------------------
chimpanzeeZO-1     CGGCGTCACCCCCTCCAACCGCGGCAGCCTCCTGCCGCTCAAGAGGAAGCTGTGGGTAAC
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mouseZO-1          GTCCCCGGGAGATGTTTATGCGGACGGTGGCGTGAGGAGCGGGCGGGCCGGCGGCGCGGA
ratZO-1            ------------------------------------------------------------
dogZO-1            ------------------------------------------------------------
chimpanzeeZO-1     GCCATCCTCTGAAAATCCTAATGGTGCTACTTCTAGTGTCAGCCAAGGAAAACCCTCTTT

mouseZO-1          GTTTCGGGTCCGAGGAGCTTCGCGCGGGCGCGGAGAGAGACAAGATGTCCGCCAGGGCCGC
ratZO-1            ------------------------------------------------------------
dogZO-1            ----------------------------------GAGAGAGACAAGATGTCCGCCAGAGCTGC
chimpanzeeZO-1     AAGACGAATTAAAGGGAGATTACACAGAA---GCAAAAGCCTTGATAGCATGGATTTCTGT

mouseZO-1          GGCCGCTAAGAGCACAGCAATGGAGGAAACAGCTATATGGGAACAGCACACAGTGACGCT
ratZO-1            --------AGAGCACAGCAATGGAGGAAACAGCTATATGGGAACAGCACACAGTGACGCT
dogZO-1            GGCCGCCAAGAACACAGCAATGGAGGAAACAGCTATATGGGAACAACACACAGTGACGCT
chimpanzeeZO-1     GAGC-TCACTAGCACAGCAATGGAGGAAACAGCTATATGGGAACAACATACAGTGACGCT
                           * ********************************** ** **********

mouseZO-1          TCACAGGGCTCCTGGGTTTGGATTTGGAATTGCAATCTCTGGTGGAAGAGATAATCCTCA
ratZO-1            TCACAGGGCTCCTGGGTTTGGATTTGGAATTGCAATATCTGGTGGAAGAGATAATCCTCA
dogZO-1            TCACAGGGCACCTGGATTTGGATTTGGAATTGCAATATCTGGTGGAAGAGATAACCCTCA
chimpanzeeZO-1     TCACAGGGCTCCTGGATTTGGGTTTGGAATTGCAATATCTGGTGGACGAGATAATCCTCA
                   ********* ***** ***** ************** ********* ******* *****

mouseZO-1          TTTTCAGAGTGGGGAAACCTCCATAGTGATTTCTGATGTGTTAAAAGGAGGGCCAGCTGA
ratZO-1            TTTTCAGAGTGGGGAAACCTCCATAGTGATTTCTGATGTGCTAAAAGGAGGGCCAGCTGA
dogZO-1            TTTTCAGAGTGGAGAAACTTCCATAGTAATTTCAGATGTGCTGAAAGGGGGACCTGCTGA
chimpanzeeZO-1     TTTTCAGAGTGGGGAAACGTCAATAGTGATTTCAGATGTGCTGAAAGGAGGACCAGCTGA
                   ************ ***** ** ***** ***** ****** * ***** ** ** *****

mouseZO-1          AGGACAGCTACAGGAAAATGACCGAGTTGCAATGGTTAACGGAGTTTCAATGGATAACGT
ratZO-1            AGGACAGCTACAGGAAAATGACCGAGTCGCAATGGTTAACGGAGTTTCAATGGATAATGT
dogZO-1            AGGACAGCTACAGGAAAATGACCGAGTTGCAATGGTTAATGGAGTTTCAATGGATAATGT
chimpanzeeZO-1     AGGACAGCTACAGGAAAATGACCGAGTTGCAATGGTTAACGGAGTTTCAATGGATAATGT
                   *************************** *********** ***************** **

mouseZO-1          TGAACATGCTTTTGCTGTTCAGCAGCTAAGGAAGAGTGGGAAAAACGCAAAAATTACTAT
ratZO-1            TGAACATGCTTTTGCTGTTCAGCAGCTAAGGAAAAGTGGGAAAAACGCAAAAATTACCAT
dogZO-1            TGAACATGCGTTTGCTGTTCAGCAACTAAGGAAAAGTGGGAAGAATGCAAAAATTACCAT
chimpanzeeZO-1     TGAACATGCTTTTGCTGTTCAGCAACTAAGGAAAAGTGGGAAAAATGCAAAAATTACAAT
                   ********* ************** ******** ******** ** ********** **

mouseZO-1          CCGAAGGAAGAAGAAAGTTCAGATCCCTGTAAGTCACCCAGATCCTGAGCCGGTGTCTGA
ratZO-1            CCGAAGAAAGAAGAAAGTTCAGATTCCTGTAAGTCACCCAGACCCTGACCCAGTGTCTGA
dogZO-1            TCGGAGAAAGAAGAAAGTTCAGATACCAGTTAGTCGTCCTGATCCTGAACCAGTGTCTGA
chimpanzeeZO-1     TAGAAGGAAGAAGAAAGTTCAAATACCAGTAAGTCGTCCTGATCCTGAACCAGTATCTGA
                     * ** ************** ** ** ** ****  ** ** ***** ** ** *****

mouseZO-1          TAATGAAGACGATAGTTATGACGAAGAAGTGCATGACCCAAGAGCTGGCCGCGGTGCTTT
ratZO-1            TAATGAAGATGATAGCTATGACGAGGATGTGCACGATCCAAGAAGTGGCCGAGGTGCCCT
dogZO-1            GAATGAAGA---TAGTTATGATGAGGAAGTCCATGACCCAAGAAGCAGCCGTGGTGGTCT
chimpanzeeZO-1     TAATGAAGAAGATAGTTATGATGAGGAAATACATGATCCAAGAAGTGGCCGGAGTGGTGT
                    ********   *** ***** ** **  * ** ** ******    ****  ***   *

mouseZO-1          AGCGAACAGAAGGAGCGAGAAGAGCTGGGCAAGGGATAGGAGTGCAAGCAGGGAGAGGAG
ratZO-1            AGCTAACAGAAGGGGTGAGAAGAGCTGGGCAAGGGATAGAAGCGCAAGCAGGGACCGGAG
dogZO-1            GGTCAGTAGAAGGAGTGAGAAGAGTTGGGCAAGGGACAGGAGTGCAAGCAGAGAGAGGAG
chimpanzeeZO-1     GGTTAACAGAAGGAGTGAGAAGATTTGGCCGAGGGATAGAAGTGCAAGTAGAGAGAGGAG
                    *  *  ****** * *******  *** * ***** ** ** ***** ** **  ****

mouseZO-1          CCTGTCCCCTCGCTCGGACAGGCGGTCCGTGGCCTCCAGTCAGCCCGCAAAGCCCACCAA
ratZO-1            CCTGTCCCCTCGCTCAGACAGGCGATCAGTGGCCTCCAGTCAGCCCGCCAAACCCACCAA
dogZO-1            TTTGTCTCCACGGTCTGATAGGCGATCTGTGGCCTCCAGTCAACCTCCCAAACCTACCAA
chimpanzeeZO-1     CTTGTCCCCGCGGTCAGACAGGCGGTCAGTGGCTTCCAGCCAGCCCGCTAAACCTACTAA
                     **** ** ** ** ** ***** ** ***** ***** ** **  * ** ** ** **

mouseZO-1          GGTCACACTGGTGAAGTCTCGGAAAAATGAAGAATATGGTCTTCGACCGGCCAGCCACAT
ratZO-1            GGTCACATTGGTGAAGTCTCGGAAAAATGAAGAATATGGTCTTCGATTGGCCAGCCATAT
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dogZO-1           AGTCACATTGGTGAAATCCCGGAAAAATGAAGAATATGGTCTTCGATTGGCCAGCCATAT
chimpanzeeZO-1    AGTCACACTGGTGAAATCCCGGAAAAATGAAGAATATGGTCTTCGATTGGCAAGCCATAT
                   ****** ******* ** ***************************  *** ***** **

mouseZO-1         ATTTGTAAAGGAAATTTCACAAGATAGTTTGGCAGCAAGAGATGGTGACATTCAAGAAGG
ratZO-1           ATTTGTAAAGGAAATTTCACAAGATAGTTTGGCAGCAAGAGATGGTAACATTCAAGAAGG
dogZO-1           ATTTGTAAAGGAAATTTCACAAGATAGTTTGGCAGCAAGAGATGGCAATATTCAAGAAGG
chimpanzeeZO-1    ATTTGTTAAGGAAATTTCACAAGATAGTTTGGCAGCAAGAGATGGCAATATTCAAGAAGG
                  ****** ************************************  * ***********

mouseZO-1         GGATGTTGTCTTGAAGATAAATGGTACTGTGACAGAAAATATGTCATTGACAGATGCAAA
ratZO-1           GGATGTTGTCCTGAAGATAAATGGTACTGTGACAGAAAATATGTCACTGACAGATGCAAA
dogZO-1           CGATGTTGTATTAAAGATAAATGGTACTGTGACAGAAAATATGTCACTGACAGATGCAAA
chimpanzeeZO-1    TGATGTTGTATTGAAGATAAATGGTACTGTGACAGAAAATATGTCATTGACAGATGCAAA
                   ********  * ********************************** ************

mouseZO-1         AACACTGATAGAAAGGTCTAAAGGCAAGTTAAAAATGGTAGTGCAAAGAGATGAGCGGGC
ratZO-1           AACATTGATAGAAAGGTCTAAAGGCAAGTTAAAAATGGTAGTGCAAAGAGATGAGCGGGC
dogZO-1           GACTTTGATAGAAAGATCTAAAGGCAAGTTAAAAATGGTAGTTCAAAGGGATGAACGGGC
chimpanzeeZO-1    GACATTGATAGAAAGGTCTAAAGGCAAATTAAAAATGGTAGTTCAAAGAGATGAACGGGC
                   **  ********** *********** ************** ***** ***** *****

mouseZO-1         TACCTTACTGAACGTCCCTGACCTTTCGGATAGTATCCATTCTGCTAATGCCTCGGAAAG
ratZO-1           TACCTTATTGAATGTCCCTGATCTTTCAGATAGTATCCATTCTGCTAATGCCTCTGAAAG
dogZO-1           TACCCTATTGAATGTCCCTGATCTTTCTGACAGTATCCACTCTGCTAATGCTTCTGAGAG
chimpanzeeZO-1    TACGCTATTGAATGTCCCTGATCTTTCTGACAGCATCCACTCTGCTAATGCCTCTGAGAG
                  ***  ** **** ******** ***** ** ** ***** ********** ** ** **

mouseZO-1         AGATGACATTTCAGAAATTCAGTCACTAGCGTCAGACCATTCAGGTCGCTCGCATGACAG
ratZO-1           AGATGACATTTCAGAAATTCAGTCACTAGCATCAGACCATTCAGTTCGCTCCCATGACAG
dogZO-1           AGATGATATTTCAGAAATTCAGTCACTGGCATCAGATCATTCTGGTCGATCACATGATAG
chimpanzeeZO-1    AGACGACATTTCAGAAATTCAGTCACTGGCATCAGATCATTCTGGTCGATCACACGATAG
                  *** ** ******************** ** ***** ***** * *** ** ** ** **

mouseZO-1         GCCACCCCGCCGCAGCCAGTCACGATCTCCTGACCAACGTTCAGAGCCCTCCGATCATTC
ratZO-1           GCCTCCCCGCCGAAGCCAGTCACGATCTCCCGACCAACGTTCAGAGCCCTCTGATCATTC
dogZO-1           ACCTCCCCGCCACAGCCGGTCACGGTCACCTGACCAACGATCAGAGCCTTCTGATCATTC
chimpanzeeZO-1    GCCTCCCCGCCGCAGCCGGTCACGATCTCCTGACCAGCGGTCAGAGCCTTCTGATCATTC
                   ** *******  **** ****** ** ** ***** ** ******** ** ********

mouseZO-1         CACGCAGTCTCCACAGCAGCCCAGCAATGGCAGTCTCCGGAGCAGAGAGGAAGAGCGAAT
ratZO-1           CACACAGTCTCCACAGCAGCCCAGCAATGGCAGTCTCCGGAGCAGAGAGGAAGAGCGCAT
dogZO-1           CAGACACTCTCCACAGCAGCCCAGCAGTGGCAGTCTCCGGAGCAGAGAGGAAGAGAGAAT
chimpanzeeZO-1    CAGGCACTCGCCACAGCAGCCAAGCAATGGCAGTCTCCGGAGTAGAGATGAAGAGAGAAT
                  **  ** ** ************ **** *************** ***** ****** * **

mouseZO-1         GTCTAAACCTGGGGCCATCTCAACTCCTGTAAAACATGTAGACGATCATCCACCCAAAGC
ratZO-1           GTCTAAACCCGGGGCTGTCTCAACTCCTGTAAAACATGTAGATGATCATACACCCAAAGC
dogZO-1           TTCTAAACCTGGGGCTGTCTCAACTCCTGTAAAGCATGCAGATGATCATACACATAAAAC
chimpanzeeZO-1    TTCTAAACCTGGGGCTGTCTCAACTCCTGTAAAGCATGCTGATGATCACACACCTAAAAC
                   ******** *****  ***************** ****  ** *****  ***  *** *

mouseZO-1         AGTGGAAGAAGTTACAGTTGAGAAAAATGAGAAGCAGACGCCCACTCTTCCAGAACCGAA
ratZO-1           AGTGGAAGAAGTTACAGTTGAAAAACATGAGAAGCAGACACCCACTCTTCCAGAACCAAA
dogZO-1           AGTAGAAGAAGTTGTAGTTGAGAGAAATGAGAAACAAGCACCCAGTCTTCCAGAACCAAA
chimpanzeeZO-1    AGTGGAAGAAGTTACAGTTGAAAGAAATGAGAAACAAACACCTTCTCTTCCAGAACCAAA
                  *** *********  ****** * * ******* **  * **   ************ **

mouseZO-1         ACCTGTGTATGCTCAAGTTGGACAACCAGATGTGGATTTACCCGTCAGCCCTTCTGATGG
ratZO-1           ACCTGTATATGCTCAAGTCGGACAGCCAGATGTGGATTTACCTGTCAGCCCTTCTGATGG
dogZO-1           GCCTGTGTATGCTCAAGTTGGACAACCAGATGTGGATTTACCTGTCAGTCCATCTGATGG
chimpanzeeZO-1    GCCTGTGTATGCCCAAGTTGGGCAGCCAGATGTGGATTTACCTGTCAGTCCATCTGATGG
                   ***** ***** ***** ** ** ****************** ***** ** ********

mouseZO-1         TGCTCTGCCTAATTCAGCTCATGAAGACGGGATACTTAGGCCCAGCATGAAACTGGTAAA
ratZO-1           TGTTCTGCCAAATTCAACACATGAAGATGGGATTCTTAGGCCCAGCATGAAACTGGTAAA
dogZO-1           CGTCCTACCTAATTCAACTCATGAAGATGGGATTCTCCGGCCCAGCATGAAATTGGTAAA
chimpanzeeZO-1    TGTCCTACCTAATTCAACTCATGAAGATGGGATTCTTCGGCCCAGCATGAAATTGGTAAA
                   *  ** ** ****** * ******** ***** **  ************** *******
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mouseZO-1           ATTCAGAAAAGGAGATAGTGTGGGTTTGCGACTAGCTGGTGGAAATGATGTCGGAATATT
ratZO-1             ATTCAGAAAAGGAGATAGTGTGGGTTTGCGACTAGCTGGTGGAAATGATGTCGGAATATT
dogZO-1             ATTCAGAAAAGGAGATAGTGTGGGCCTGCGCCTGGCTGGTGGAAATGATGTTGGAATATT
chimpanzeeZO-1      ATTCAGAAAAGGAGATAGTGTGGGTTTGCGGCTGGCTGGTGGAAATGATGTTGGAATATT
                    ************************  **** ** ***************** ********

mouseZO-1           TGTAGCTGGCGTTCTAGAAGATAGCCCTGCAGCCAAAGAAGGCTTAGAGGAAGGTGATCA
ratZO-1             TGTAGCTGGCGTTCTAGAAGATAGCCCTGCAGCCAAAGAAGGCTTAGAGGAAGGTGATCA
dogZO-1             TGTAGCTGGTGTTCTAGAAGATAGCCCTGCAGCCAAAGAAGGCTTAGAAGAGGGTGATCA
chimpanzeeZO-1      TGTAGCTGGCGTTCTAGAAGATAGCCCTGCAGCCAAGGAAGGCTTAGAGGAAGGTGATCA
                    ********* ************************* ********** ** ********

mouseZO-1           AATTCTCAGGGTGAACAATGTAGATTTCACAAATATCATAAGGGAAGAGGCCGTCCTTTT
ratZO-1             AATTCTCAGGGTGAACAATGTAGATTTCACAAATATCATAAGAGAAGAAGCTGTTCTTTT
dogZO-1             AATTCTCAGGGTAAACAATGTAGATTTCACAAACATCATAAGAGAAGAAGCCGTCCTTTT
chimpanzeeZO-1      AATTCTCAGGGTAAACAACGTAGATTTTACAAATATCATAAGAGAAGAAGCCGTCCTTTT
                    ************ ***** ******** ***** ******** ***** ** ** *****

mouseZO-1           CCTCCTTGACCTCCCTAAAGGTGAAGAAGTGACCATACTGGCTCAGAAGAAGAAGGACGT
ratZO-1             CCTCCTCGACCTCCCTAAAGGTGAAGAAGTGACCATATTGGCTCAGAAGAAAAAGGACGT
dogZO-1             CCTACTCGACCTCCCTAAAGGAGAAGAAGTGACCATATTGGCTCAGAAGAAGAAAGATGT
chimpanzeeZO-1      CCTGCTTGACCTCCCTAAAGGAGAAGAAGTGACCATATTGGCTCAGAAGAAGAAGGATGT
                    *** ** ************** ************** ************* ** ** **

mouseZO-1           TTATCGCCGCATTGTAGAATCAGATGTAGGAGATTCATTCTATATTAGAACGCATTTTGA
ratZO-1             TTATCGCCGCATTGTAGAGTCAGATGTAGGAGACTCGTTCTATATTAGAACACATTTTGA
dogZO-1             TTATCGTCGCATTGTAGAATCAGATGTGGGAGATTCTTTCTATATTAGAACCCACTTTGA
chimpanzeeZO-1      TTATCGTCGCATTGTAGAATCAGATGTAGGAGATTCTTTCTATATTAGAACCCATTTTGA
                    ****** *********** ******** ***** ** ************** ** *****

mouseZO-1           ATATGAAAAAGAATCTCCTTACGGACTTAGTTTTAACAAAGGAGAGGTGTTCCGGGTCGT
ratZO-1             ATATGAGAAAGAATCTCCTTATGGACTCAGTTTTAACAAAGGAGAGGTGTTCCGGGTCGT
dogZO-1             ATATGAAAAGGAATCTCCCTACGGACTTAGTTTTAACAAAGGAGAGGTGTTTCGTGTTGT
chimpanzeeZO-1      ATATGAAAAGGAATCTCCCTATGGACTTAGTTTTAACAAAGGAGAGGTGTTCCGTGTTGT
                    ****** ** ******** ** ***** ************************ ** ** **

mouseZO-1           GGATACTTTATACAATGGAAAGCTGGGCTCTTGGCTTGCCATTCGAATTGGCAAAAATCA
ratZO-1             GGACACCCTGTACAACGGGAAGCTGGGCTCCTGGCTGGCCATTCGAATTGGCAAAAATCA
dogZO-1             GGATACCTTGTACAATGGGAAACTAGGCTCTTGGCTCGCTATTCGAATTGGCAAAAATCA
chimpanzeeZO-1      GGATACCTTGTACAATGGAAAACTGGGCTCTTGGCTTGCTATTCGAATTGGTAAAAATCA
                    *** **  * ***** ** ** ** ***** ***** ** ********** ********

mouseZO-1           TAAGGAGGTAGAACGAGGCATCATCCCAAATAAGAACAGAGCTGAACAGTTAGCCAGTGT
ratZO-1             CAAGGAGGTAGAGCGAGGCATCGTTCCTAATAAGAACAGAGCCGAGCAGTTAGCCAGTGT
dogZO-1             TAAAGAAGTAGAACGAGGCATCATCCCTAATAAGAACAGGGCTGAGCAGTTAGCCAGTGT
chimpanzeeZO-1      TAAGGAGGTAGAACGAGGCATCATCCCTAATAAGAACAGAGCTGAGCAGCTAGCCAGTGT
                     ** ** ***** ********* * ** ********** ** ** *** **********

mouseZO-1           ACAGTACACACTTCCAAAGACAGCGGGTGGTGATCGGGCAGACTTCTGGAGGTTTCGAGG
ratZO-1             ACAGTACACACTTCCAAAGACAGCAGGTGGCGATCGGGCAGACTTCTGGAGGTTTCGAGG
dogZO-1             ACAGTACACACTTCCAAAAACAGCTGGGGGAGACCGTGCTGACTTCTGGAGATTCCGGGG
chimpanzeeZO-1      ACAGTATACACTTCCAAAAACAGCAGGCGGAGACCGTGCTGACTTCTGGAGATTCAGAGG
                    ****** *********** ***** ** ** ** ** ** *********** **  * **

mouseZO-1           TCTTCGCAGCTCCAAGAGAAATCTTCGAAAAAGCAGAGAGGACTTGTCAGCTCAGCCAGT
ratZO-1             TCTTCGTAGCTCCAAGAGAAATCTTCGAAAAAGCAGAGAGGACCTGTCAGCGCAGCCAGT
dogZO-1             TCTTCGCAGCTCCAAGAGAAATCTTCGAAAGAGTAGAGAGGATTTGTCAGCTCAGCCAGT
chimpanzeeZO-1      TCTTCGCAGCTCCAAGAGAAATCTTCGAAAAAGCAGAGAGGATTTGTCCGCTCAGCCTGT
                    ****** ********************** ** ********  **** ** ***** **

mouseZO-1           TCAAACTAAGTTCCCAGCTTATGAAAGGGTTGTTCTTCGAGAAGCTGGATTCCTAAGACC
ratZO-1             TCAAACAAAGTTCCCAGCTTATGAAAGGGTTGTTCTTCGAGAAGCTGGATTCCTAAGACC
dogZO-1             TCAAACAAAGTTTCCAGCCTATGAAAGAGTTGTTCTTCGAGAAGCTGGATTTCTGAGGCC
chimpanzeeZO-1      TCAAACAAAGTTTCCAGCTTATGAAAGAGTGGTTCTTCGAGAAGCTGGATTTCTGAGGCC
                    ****** ***** ***** ******** ** ******************** ** ** **

mouseZO-1           TGTAACCATCTTTGGACCAATAGCTGATGTTGCCAGAGAAAAGTTGGCAAGAGAGGAGCC
ratZO-1             TGTAACCATCTTTGGACCGATTGCTGATGTTGCCAGAGAAAAGTTAGCAAGGGAGGAGCC
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dogZO-1           TGTAACTATCTTTGGACCCATAGCTGATGTTGCCAGAGAAAAGCTGGCAAGAGAAGAACC
chimpanzeeZO-1    TGTAACCATTTTTGGACCAATAGCTGATGTTGCCAGAGAAAAGCTGGCAAGAGAAGAACC
                  ****** ** ******** ** ********************** * ***** ** ** **

mouseZO-1         AGATATCTATCAGATTGCAAAAAGTGAACTACGAGACGCTGGGACTGACCATCGTAGCTC
ratZO-1           AGACATTTATCAGATTGCAAAAAGTGAACCACGAGATGCTGGAACTGACCATCGGAGCTC
dogZO-1           AGATATTTATCAGATTGCAAAAAGTGAACCACGAGATGCTGGAACTGATCAACGTAGCTC
chimpanzeeZO-1    AGATATTTATCAAATTGCAAAGAGTGAACCACGAGACGCTGGAACTGACCAACGTAGCTC
                  *** ** ***** ******** ******* ****** ***** ***** ** ** *****

mouseZO-1         TGGCATCATTCGCCTTCATACAATAAAGCAAATCATAGATCAGGATAAACATGCTTTATT
ratZO-1           GGGCATTATTCGCCTTCATACAATAAAGCAAATCATAGATCAAGATAAACATGCTTTATT
dogZO-1           TGGTATTATTCGTCTTCATACAATAAAACAAATAATAGATCAGGACAAACATGCTTTATT
chimpanzeeZO-1    TGGCATTATTCGCCTGCATACAATAAAGCAAATCATAGATCAAGACAAACATGCTTTATT
                   ** ** ***** ** ********** ***** ******** ** **************

mouseZO-1         AGATGTAACGCCAAATGCGGTTGATCGTCTTAATTATGCGCAGTGGTATCCAATTGTTGT
ratZO-1           AGATGTCACACCAAATGCAGTCGATCGCCTTAATTATGCACAGTGGTATCCGATTGTTGT
dogZO-1           AGATGTAACACCAAATGCAGTTGATCGTCTGAATTATGCCCAGTGGTATCCAATTGTAGT
chimpanzeeZO-1    AGATGTAACACCAAATGCAGTTGATCGTCTTAACTATGCCCAGTGGTATCCAATTGTTGT
                  ****** ** ******** ** ***** ** ** ***** ********** ***** **

mouseZO-1         GTTCCTTAACCCTGACTCTAAGCAAGGTGTAAAAACAATGAGGATGAGGTTGTGTCCGGA
ratZO-1           GTTCCTTAACCCTGACTCTAAGCAGGGTGTAAAAACAATGAGGATGAGGCTATGTCCAGA
dogZO-1           ATTCCTTAACCCTGATTCTAAGCAAGGTGTGAAAACTATGAGGATGAGGCTATGCCCAGA
chimpanzeeZO-1    ATTTCTTAACCCTGATTCTAAGCAAGGAGTAAAAACAATGAGAATGAGGTTATGTCCAGA
                   ** ********** ******** ** ** ***** ***** ****** * ** ** **

mouseZO-1         GTCTCGGAAAAGCGCCAGGAAGCTATATGAACGCTCTCATAAGCTTCGTAAGAACAATCA
ratZO-1           GTCTCGGAAAAGTGCCAGGAAGCTATATGAACGGTCTCATAAACTTCGTAAAAATAATCA
dogZO-1           ATCTCGAAAAAGTGCCAGGAAATTATATGAACGGTCTCATAAACTTCGTAAAAATAATCA
chimpanzeeZO-1    ATCTCGGAAAAGTGCCAGGAAGTTATATGAGCGATCTCATAAACTTCGTAAAAATAATCA
                   ***** ***** ********  ******* ** ******** ******** ** *****

mouseZO-1         CCATCTCTTCACAACTACAATTAACTTAAACTCAATGAATGATGGTTGGTACGGTGCCCT
ratZO-1           CCATCTTTTTACAACCACAATTAACTTAAACTCAATGAATGATGGTTGGTATGGTGCCCT
dogZO-1           CCATCTTTTTACAACTACAATTAACTTAAATTCAATGAATGATGGTTGGTATGGTGCATT
chimpanzeeZO-1    CCATCTTTTTACAACTACAATTAACTTAAATTCAATGAATGATGGTTGGTATGGTGCGCT
                  ****** ** ***** ********** ********** ***** *

mouseZO-1         GAAAGAAGCGATTCAGCAGCAACAGAACCAGCTGGTGTGGGTCTCTGAGGGGAAGGCGGA
ratZO-1           GAAAGAAGCGATTCAGCAGCAACAGAACCAGCTGGTGTGGGTCTCTGAGGGGAAGGCGGA
dogZO-1           GAAAGAAGCAATTCAGCAGCAACAGAACCAGTTGGTATGGGTTTCTGAGGGAAAGGCGGA
chimpanzeeZO-1    GAAAGAAGCAATTCAACAACAGCAAAACCAGCTGGTATGGGTTTCCGAGGGAAAGGCGGA
                  ********* ***** ** ** ** ****** **** ***** ** ***** ********

mouseZO-1         TGGTGCTACAAGTGATGACCTTGATTTGCATGACGATCGTCTGTCCTACCTGTCAGCCCC
ratZO-1           TGGTGCTACAAGTGATGACCTTGATTTGCATGATGATCGTCTGTCCTACCTGTCAGCCCC
dogZO-1           TGGTGCTACAAGTGATGACCTTGATTTGCATGATGATCGTCTCTCCTACCTGTCAGCCCC
chimpanzeeZO-1    TGGTGCTACAAGTGATGACCTTGATTTGCATGATGATCGTCTGTCCTACCTGTCAGCTCC
                  ********************************** ******** ********** **

mouseZO-1         AGGTAGTGAGTACTCAATGTATAGCACGGACAGTAGACACACTTCTGACTATGAAGACAC
ratZO-1           AGGTAGTGAGTACTCAATGTATAGCACGGACAGTAGACACACTTCTGACTATGAAGACAC
dogZO-1           AGGTAGTGAATACTCAATGTATAGCACGGACAGTAGACACACTTCTGACTATGAAGACAC
chimpanzeeZO-1    AGGTAGTGAATACTCAATGTATAGCACGGACAGTAGACACACTTCTGACTATGAAGACAC
                  ********* **************************************************

mouseZO-1         AGATACAGAAGGCGGGGCCTACACTGATCAAGAACTAGATGAAACTCTTAATGATGAGGT
ratZO-1           AGATACAGAAGGCGGGGCCTACACTGATCAAGAACTAGATGAAACTCTTAATGATGAGGT
dogZO-1           AGATACAGAAGGCGGGGCCTACACTGATCAAGAACTAGATGAAACTCTTAATGATGAGGT
chimpanzeeZO-1    AGACACAGAAGGCGGGGCCTACACTGATCAAGAACTAGATGAAACTCTTAATGATGAGGT
                  *** ********************************************************

mouseZO-1         GGGGACTCCCCCGGAGTCTGCCATTACACGGTCCTCTGAGCCTGTAAGAGAGGATTCCTC
ratZO-1           GGGGACTCCACCGGAGTCTGCTATTACACGGTCCTCTGAGCCTGTAAGAGAGGATTCCTC
dogZO-1           TGGGACTCCACCGGAGTCTGCCATTACACGGTCCTCTGAGCCTGTAAGAGAGGACTCCTC
chimpanzeeZO-1    TGGGACTCCACCGGAGTCTGCCATTACACGGTCCTCTGAGCCTGTAAGAGAGGACTCCTC
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mouseZO-1          TGGAATGCATCATGAAAACCAGACATACCCTCCTTACTCACCACAAGCGCAGCCACAAGC
ratZO-1            TGGAATGCATCATGAAAACCAAACATATCCTCCTTACTCACCACAAGCGCAGCCACAAGC
dogZO-1            TGGAATGCATCATGAAAACCAAACATATCCTCCTTATTCACCACAAGCGCAGCCACAACC
chimpanzeeZO-1     TGGAATGCATCATGAAAACCAAACATATCCTCCTTACTCACCACAAGCGCAGCCACAACC
                   ********************** ***** ******** ********************** *

mouseZO-1          TATTCATAGAATAGACTCCCCTGGACTTAAGCCAGCCTCTCAACAGAAAGCAGAAGCCTC
ratZO-1            TATTCATAGAATAGACTCCCCTGGACTTAAGACAGCCTCTCAACAGAAAGCAGAAGCCTC
dogZO-1            AATTCATAGAATAGACTCCCCTGGATTTAAAACAGCTTCTCAACAGAAAGCAGAAGCCTC
chimpanzeeZO-1     AATTCATAGAATAGACTCCCCTGGATTTAAGCCAGCCTCTCAACAGAAAGCAGAAGCTTC
                    ************************* ****  **** ******************** **

mouseZO-1          ATCTCCAGTCCCTTACCTTTCGCCTGAAACAACCCCAGCATCATCAGCCTCTGCAGTTAA
ratZO-1            ATCTCCAGTCCCTTACCTTTCGCCTGAAACAAACCCAGCATCATCAGCCTCTGCAGTTAA
dogZO-1            ATCTCCAGTCCCTTACCTTTCGCCTGAAACAAACCCAGCATCATCAACCTCTGCTGTTAA
chimpanzeeZO-1     ATCTCCAGTCCCTTACCTTTCGCCTGAAACAAACCCAGCATCATCAACCTCTGCTGTTAA
                   ******************************** ************ ******* *****

mouseZO-1          TCATAATGTCAGTGTAACTAATGTCAGCCTGGAGGAGCCTGCCCCAGCCCCTCCCACCTC
ratZO-1            GCATAATGTAAATTTAACTAATGTCAACCTGGAGGAGCCCACCCCAGCTCCTCCCACCTC
dogZO-1            CCATAATGTAACTTTAACTAATGTCAGACTGGAGGGGCCTACCCCAGCTCCTTCTACTTC
chimpanzeeZO-1     TCATAATGTAAATTTAACTAATGTCAGACTGGAGGAGCCCACCCCAGCTCCTTCCACCTC
                    ******** * * ************  ******* ***  ******* *** * ** **

mouseZO-1          GCACGCATCACAGCCTGGTTGTTTAGGAGCACCAAGTGCTGAGGCAGCTCACGTAGGTCT
ratZO-1            GCACGTATCACAAGCTGATTGTTTAGGAGCACCAAGTCCTGAGGCACCTCACACGATGCT
dogZO-1            TTACTCACCACAAGCTGATTCTTTAAGAACACCAAGCACTGAGGCAGCTCACATAATGCT
chimpanzeeZO-1     TTACTCACCACAAGCTGATTCTTTAAGAACACCAAGTACTGAGGCAGCTCACATAATGCT
                     **  * ****  *** ** **** ** *******  ******** *****      **

mouseZO-1          CAGAGGTGAAGGACCACCATTGCCGCCGCATGCAGACCCAGCAAAGGTGTACAGGAAGGA
ratZO-1            CAGAGACGAAGGAGTGTCATTGCCGTCGCATGTAGACCCAGCAAAGGTATATAGGAAGGA
dogZO-1            AAGAGATCAAGAGCCATCATTGCCGTCGCATGTAGAGCCAGCAAAGGTGTATAGAAAAGA
chimpanzeeZO-1     AAGAGATCAAGAACCATCATTGTCGTCGCATGTAGATCCAACAAAGGTGTATAGAAAGGA
                    ****   ***      ***** ** ****** *** *** ******* ** ** ** **

mouseZO-1          GCCATATTCTGAAGAAATGATGAGACAAAACCATATTTTAAAACAACCAGCTCTTGGTCA
ratZO-1            GCCATATCCTGAGGAAATGATGAGACAAAACCATATTTTAAAACAGCCAGCTCTTGGTCA
dogZO-1            TCCCTATCCTGAGGAAATGATGAGACAGAACCATGTTTTGAAACAGCCAGCTGTTGGTCA
chimpanzeeZO-1     TCCATATCCCGAGGAAATGATGAGGCAGAACCATGTTTTGAAACAGCCAGCCGTTAGTCA
                    ** *** * ** ********** ** ****** **** ***** *****  ** ****

mouseZO-1          CCCAGGGCAGAGGCCAGATAAAGAGCCAAATCTAGCCTATGAACCCCAACTTCCATATAT
ratZO-1            TCCAGGGCAGAGGCTGGATAAAGAGCCAAATCCAGCCTATGATCCCCAACTTCCATATGT
dogZO-1            CCCAGGGCAGAGGCCAGACAAAGAGCCTAATCTGAGCTATGAATCCCAACCCCCATATGT
chimpanzeeZO-1     CCCAGGGCACAGGCCAGACAAAGAGCCTAATCTGACCTATGAACCCCAACTCCCATACGT
                    ******** ****  ** ******** ****    ******  ******  *****  *

mouseZO-1          AGAAAAACAAGCCAGCAGAGACCTTGAGCAGCCGTCATACAGGTATGAGGTCTCAAGCTA
ratZO-1            AGAAAAACAAGCCAGCAGAGACCTTGAGCAGCCACCATACAGGTATGAGTCCTCAAGCTA
dogZO-1            AGAAAAACAGGCCAACAGAGACCTCGAGCAGCCCACATACAGATACGACTCCTCAAGCTA
chimpanzeeZO-1     AGAGAAACAAGCCAGCAGAGACCTCGAGCAGCCCACATACAGATACGAGTCCTCAAGCTA
                   *** ***** **** ********* ********  ******* ** **   *********

mouseZO-1          CACAGACCAGTTTTCTCGGAACTATGACCATCGCCTACGGTTTGAAGATCGAATCCCTAC
ratZO-1            CACAGACCAGTTTTCTCGGAACTATGACCATCGCCTACGATTTGAAGACCGAGTCCCTAC
dogZO-1            TACAGACCAGTTTTCTCGAAACTATGATCATCGTCTCCGCTATGAAGAGCGCATTCCCAC
chimpanzeeZO-1     TACGGACCAGTTTTCTCGAAACTATGAACATCGTCTGCGATACGAAGATCGCGTCCCCAT
                    ** ************** ******** ***** ** ** *  ***** **  * ** *

mouseZO-1          CTATGAAGACCAGTGGTCATATTATGATGACAAACAGCCCTACCAACCTCGGCC——TTT
ratZO-1            CTATGAAGACCAGTGGTCATATTATGATGACAAACAGCCCTACCCAACTCGGCC——CTT
dogZO-1            ATATGAAGAGCAGTGGTCATATTACGATGACAAACAGCCCTACCAGCCTCGGCCTTCTCT
chimpanzeeZO-1     GTATGAAGAACAGTGGTCATATTATGATGACAAACAGCCCTACCCATCTCGGCCACCTTT
                    ******** ************** ********************   *******     *

mouseZO-1          TGAGAATCAGCATCCCCGAGACCTGGACTCCAGACAACATCCCGAAGAGGCTTCAGAACG
ratZO-1            TGATACTCAGCATCCTCGAGACTTGGACTCCAGACAGCATCCTGAAGAGGCTTCAGAACG
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dogZO-1           TGATAATCAGCACCCTCGGGACCTTGACTCCAGACAGCATCCAGAAGAGTCCTCAGAAAG
chimpanzeeZO-1    TGATAATCAGCACTCTCAAGACCTTGACTCCAGACAGCATCCCGAAGAGTCCTCAGAACG
                  *** * ******  * *  *** * ********** ***** ****** * ****** *

mouseZO-1         AGGTTATTTCCAGCGTTTTGAAGAGCCAGCCCCTCTGTCGTACGACAGTAGAACACGCTA
ratZO-1           AGGCTATTTCCAGCGTTTTGAAGAGCCCGCCCCTCTGCCATATGACAGTAGACCACGCTA
dogZO-1           AGGGTCTTACCCACGTTTTGAAGAGCCAGCCCCTCTGTCCTATGACAGCAGACCACGCTA
chimpanzeeZO-1    AGGGTACTTTCCACGTTTTGAAGAGCCAGCCCCTCTGTCTTACGACAGCAGACCACGTTA
                  *** *  *  * ********** ********* * ** ***** *** **** **

mouseZO-1         TGAGCAGCTGCCTCGAACCTCTACTCTACGACATGAAGAGCAGCCAGCCCCTGCATATGA
ratZO-1           CGAGCAGCTGCCTCGAACCTCTACTCTCCGACATGAAGAACAGCCAACCAGTGGATATGA
dogZO-1           TGACCAGCCACCTAGAACCTCTACCCTACGACACGAAGAGCAACCAACTCCTGGATATGA
chimpanzeeZO-1    CGAACAGGCACCTAGAGCATCCGCCCTGCGGCACGAAGAGCAGCCAGCTCCTGGGTATGA
                   ** ***   *** ** * **  * ** ** ** ***** ** *** *   **  *****

mouseZO-1         GGTGCACAACAGGTACAGGCCAGAGGCACAGCCCTATTCTTCAACAGGCCCTAAGTCATC
ratZO-1           GGTGCACAACAGGTACAGGCCAGAAGCACAGCCCTATGCTCCAGCAGGTCCTAAGTCATC
dogZO-1           CATGCATAACAGATACAGACCAGAAGCGCAGTCCTATTCTTCAGCAGGCCCTAAGGCATC
chimpanzeeZO-1    CACACATGGTAGACTCAGACCGGAAGCCCAGCCCCACCCTTCAGCAGGGCCCAAGCCCGC
                      **    **   *** ** ** ** *** ** *  ** ** **** ** *** *  *

mouseZO-1         TGAGCCCAAGCAGTACTTTGACCAGTACCCGCGAAGTTATGAGCAAGTTCCACCACCAGG
ratZO-1           TGAGCCGAAGCAGTACTTTGACCAGTACCCACGAAGTTATGAGCAAGTACCACCACCAGG
dogZO-1           TGAACCGAAGCAGTATTTTGACCAGTACCCACGAAGTTACGAGCAAGTACCATCACAGGG
chimpanzeeZO-1    AGAGTCCAAGCAGTATTTTGAGCAATATTCACGCAGTTACGAGCAAGTACCACCCCAAGG
                   **  * ******** ***** ** **  * ** ***** ******** *** * *  **

mouseZO-1         CTTTACCTCCAAAACAGGCCATTACGAGCCTCTCCATGGTGCTGCAGTTGTCCCTCCTCT
ratZO-1           ATTTACCTCCAAAACAGGCCATTACGAGCCTCTCCATGGTGCTGCAGTTGTTCCTCCTCT
dogZO-1           ATTTTCCTCGAAAGCCGGCCACTATGAGCCTCTCCATGGTGCTGCGGTTGTCCCTCCTCT
chimpanzeeZO-1    ATTTACCTCTAGAGCAGGTCATTTTGAGCCTCTCCATGGTGCTGCAGCTGTCCCTCCGCT
                   *** **** * * * ** ** *  ********************* * *** ***** **

mouseZO-1         GATACCTTCCTCTCAACAAAAGCCAGAAGTCCTGCGCTCGGCTACCAAACCACAGCCTCC
ratZO-1           GATACCTTCCTCTCAACATAAGCCAGAAGTTCTGCCCTCAGCTACCAAGCCACAGCCTCC
dogZO-1           AATACCCGCATCTCAACATAAGCCAGAAGTTCTGCCTTCAAATACCAAACCTCTGCCTCC
chimpanzeeZO-1    GATACCTTCATCTCAGCATAAGCCAGAAGCTCTGCCTTCAAACACCAAACCACTGCCTCC
                   *****  * ***** ** **********  ****  **    ***** ** * ******

mouseZO-1         ACCCCCAACCCTAACTGAGGAGGAGGAGGATCCAGCAATGAAACCACAGTCTGTGCTCAC
ratZO-1           GCCCCCAGCCCTAACTGAGGAAGAGGAGGATCCAGCAATGAAACCACAGTCTGTGCTCAC
dogZO-1           ACCCCCAACTCTGACTGAAGAGGAGGAAGATCCAGCAATGAAACCCCAGTCTGTACTCAC
chimpanzeeZO-1    ACCCCCAACTCAAACCGAAGAAGAGGAAGATCCAGCAATGAAGCCACAGTCTGTACTCAC
                   ****** * *  ** ** ** ***** ********************** ** ******** *****

mouseZO-1         CAGAGTCAAAATGTTTGAAAACAAAAGATCTGCGTCTTTGGAGAACAAGAAAGATGTGAA
ratZO-1           CAGGGTCAAAATGTTTGAAAACAAAAGATCTGCGTCTCTGGAGAACAAGAAGGATGTGAA
dogZO-1           TAGAGTAAAAATGTTTGAAAACAAAAGATCTGCATCATTGGAGAACAAGAAGGATGAAAA
chimpanzeeZO-1    CAGAGTTAAGATGTTTGAAAACAAAAGATCTGCATCCTTAGAGACCAAGAAGGATGTAAA
                   ** ** ** ************************ **  * **** ****** ****  **

mouseZO-1         TGACACTGCCAGCTTCAAGCCTCCGGAAGTAGCATCTAAACCTCCAGGTGCTTCTCTTGC
ratZO-1           TGACACTGCCAGCTTTAAGCCTCCAGAAGTAGCATCTAAACCTCCAAGTGCTTCTCTTGT
dogZO-1           CCACACCGCTGGTTTTAAGCCTCCAGAGGTAGCTTCTAAACCTCCAGGTGCTCCCATCAT
chimpanzeeZO-1    TGACACTGGCAGTTTTAAGCCTCCAGAAGTAGCATCTAAACCTTCAGGTGCTCCCATCAT
                    **** *   * ** ******** ** ***** ********* ** ***** *  *

mouseZO-1         TGGCCCTAAACCTGTCCCTCAGAGTCAGTTTAGTGAGCACGACAAAACGCTCTACAGGCT
ratZO-1           TGGCCCTAAACCTGTTTCTCAGACTCAGTTTAGTGAGCATGACAAAACACTCTACAGGCT
dogZO-1           TGGTCCTAAACCCACTCCTCAGAATCAGTTCAGTGAACATGACAAAACACTGTACAGGAT
chimpanzeeZO-1    TGGTCCCAAACCCACTTCTCAGAATCAGTTCAGTGAACATGACAAAACTCTGTACAGGAT
                  *** ** *****     ****** ****** ***** ** ******** ** ****** *

mouseZO-1         CCCAGAGCCTCAGAAACCTCAAGTGAAGCCACCCGAAGATATTGTTCGATCAAATCATTA
ratZO-1           CCCAGAGCCTCAGAAACCTCAAGCGAAGCCACCTGAAGATATTGTTCGATCAAATCATTA
dogZO-1           CCCAGAACCTCAAAAACCTCAGATGAAGCCACCCGAAGATATTGTTCGGTCTAATCATTA
chimpanzeeZO-1    CCCAGAACCTCAAAAACCTCAACTGAAGCCACCTGAAGATATCGTTCGGTCCAATCATTA
                  ****** ***** ********   ********* ******** ***** ** ********
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mouseZO-1          CGACCCTGAAGAGGATGAAGAATATTACCGGAAACAGCTCTCCTACTTTGACCGAAGAAG
ratZO-1            CGATCCTGAAGAGGATGAAGAGTATTACCGGAAACAGCTCTCTTACTTTGACCGGAGAAG
dogZO-1            TGATCCCGAAGAGGATGAAGAATATTATCGAAAGCAGCTCTCCTACTTTGACCGAAGAAG
chimpanzeeZO-1     TGACCCTGAAGAAGATGAAGAATATTATCGAAAACAGCTGTCATACTTTGACCGAAGAAG
                    ** ** ***** ******** ***** ** ** ***** ** ********** *****

mouseZO-1          TTTTGAGAGCAAGCCTTCTGCACATCTTCCTGCTGGCCATCACTCAGAGCCTGCTAAGCC
ratZO-1            TTTCGAGAGCAAGCCTCCTGCACATATTCCTGCTGGCCATCACTCAGAGCCTGCCAAGCC
dogZO-1            TTTTGAAAACAAGCCTTCTACACACATTCCTGCTGGCCATCTCTCAGAGCCTGCCAAGCC
chimpanzeeZO-1     TTTTGAGAATAAGCCTCCTGCACACATTGCCGCCAGCCATCTCTCCGAGCCTGCAAAGCC
                   *** ** *  ****** ** ****  ** * **  ****** *** ******** *****

mouseZO-1          AGTCCATTCTCAGAGCCAGCCCAACTTCCCTAGTTACTCTTCAAAGGGAAAA——CCCGA
ratZO-1            AGTCCATTCTCAGAGTCAGCCGAATTTCTCTAGTTATTCTTCAAAGGGGAAA——CCCGA
dogZO-1            AGTTCATTCTCAGAATCAAACAAACTTTTCTAGTTATTCTTCGAAGGGAAAGTCTCCTGA
chimpanzeeZO-1     AGCTCATTCTCAGAATCAATCAAATTTTTCTAGTTATTCTTCAAAGGGAAAGCCTCCTGA
                   **  **********  **  * ** **  ******* ***** ***** **    ** **

mouseZO-1          AACTGATGCTGTGGATAGATCATTCAGTGAGAAACGTTATGATCCAGCCCAGGCCACGCC
ratZO-1            AACTGATGCTATGGATAGATCATTCAGTGAGAAACGTTATGATCCAACCCAGGCCATGCC
dogZO-1            AGCTGATGCCCCTGATAGATCATTTGGTGAGAAGCGCTATGAGCCAGTCCAGGCCACTCC
chimpanzeeZO-1     AGCTGATGGTGTGGATAGATCATTTGGCGAGAAACGCTATGAACCCATCCAGGCCACTCC
                   * ******     **********  * ***** ** ***** **   ********  **

mouseZO-1          TCCTCCTCCTCCGTTGCCCTCACAGTACAGCCAGCCAGCTCCACCTCTGTCCAGCTCTTC
ratZO-1            TCCTCCTCCTCCGTTGCCCTCACAGTACAGCCAGCCAGTTCCGCCTCTGTCCAACTCTTC
dogZO-1            CCCTCCTCCCCCCATTGCCCTCCCAGTATGCCCAGCCTTCTCAGCCCGGTACCAGCTCCTC
chimpanzeeZO-1     CCCTCCTCCTCCATTGCCCTCGCAGTATGCCCAGCCATCTCAGCCTGTCACCAGCGCGTC
                    ******** ** ******** *****   ******   **  **     *** * * **

mouseZO-1          TCT———CCACATACATTCCAAGGGCGCCCAGGGTGAAGGCAACTCAGTATCATTGGA
ratZO-1            TCT———CCACATACATTCCAAGGCCGCCCAGAGTGAAGGCAATTCCGTATCGTTGGA
dogZO-1            TCTTGCCCTCCACACGCATGCCAAGGGGGCACATGGTGAAGGTAATTCAATATCACTGGA
chimpanzeeZO-1     TCT———CCACATACATTCTAAGGGAGCACATGGTGAAGGTAATTCAGTGTCATTGGA
                   ***      *****  *** * ****  ** **  ******* ** **  * **  ****

mouseZO-1          TTTTCAGAACTCATATATGTCCAAACCAGACCCACCCCCATCTCAGAGTAAACCAGCAAC
ratZO-1            TTTTCAGAACTCATATATATCCAAACCAGACCCACCCCCATCTCAGAGCAAACCAGCAAC
dogZO-1            CTTTCAGAATTCTTTAGTGTCCAAACCAGACCCACCTCCATCACAGAATAAGCCAGCAAC
chimpanzeeZO-1     TTTTCAGAATTCCTTAGTGTCCAAACCAGACCCACCTCCATCTCAGAATAAGCCAGCAAC
                    ******** ** *   * ****************** ***** ****  ** ********

mouseZO-1          TTTCAGACCACCAACTCGAGAAGACCCCCCTCAG——ACTTTCTATCCGCAGAAAAGTTT
ratZO-1            TTTTAGACCACCAACCCGGGAGGACCCTCCTCAG——ACCTTCTATCCCCAGAAAAGTTT
dogZO-1            TTTCAGACCACCAAACCGAGAAGATACTGTTCAGTCTACTTTCTATCCACAGAAAAGTTT
chimpanzeeZO-1     TTTCAGACCACCAAACCGAGAAGATACTGCTCAGCCAGCTTTCTATCCCCAGAAAAGTTT
                   *** **********  ** ** **  *   ****    * ******** ***********

mouseZO-1          CCCAGACAAAGCTCCAGTTAACGGAGCTGAGCAGACTCAGAAAACCATCACTCCGGTGTA
ratZO-1            CCCAGACAAAGCTTCAGTTAATGGAGCTGAGCAGACTCAGAAAACCATCACTCCAGCATA
dogZO-1            CCCAGATAAAGCTCCAGTTAATGGAGCTGAACAGACTCAGAAAACGGTCACTCCAGCATA
chimpanzeeZO-1     TCCAGATAAAGCCCCAGTTAATGGAACTGAACAGACTCAGAAAACAGTCACTCCAGCATA
                    ***** *****  ******* *** **** **************  ******* *  **

mouseZO-1          CAATCGATTCACACCAAAGCCGTACACAAGTTCTGCCCGGCCATTTGAACGCAAATTTGA
ratZO-1            CAACCGATTCACACCAAAGCCGTACACGAGCTCTGCCCGGCCATTTGAACGCAAGTTTGA
dogZO-1            TAATCGATTCACACCAAAACCATACACAAGTTCTGCCCGGCCATTTGAACGCAAGTTTGA
chimpanzeeZO-1     CAATCGATTCACACCAAAACCATATACAAGTTCTGCCCGACCATTTGAACGCAAGTTTGA
                    ** ************** ** ** ** ** ******** ************** *****

mouseZO-1          AAGTCCGAAGTTCAACCATAATCTTCTGCCAAGTGAAACTGTACATAAACCTGAATTGTC
ratZO-1            AAGTCCAAAGTTCAACCATAATCTTCTGCCAAGTGAAACTGTACATAAACCTGAATTGTC
dogZO-1            AAGTCCTAAATTCAACCACAATCTCCTGCCAAGTGAAACAGCACATAAACCTGACTTGTC
chimpanzeeZO-1     AAGTCCTAAATTCAATCACAATCTTCTGCCAAGTGAAACTGCACATAAACCTGACTTGTC
                   ****** ** ***** ** ***** ************** * ************ *****

mouseZO-1          TTCAAAAACTCCCACTTCCCCAAAAACTCTTATGAAAGCTCATAGTTCAACACAGCCTCC
ratZO-1            TTCAAAACCTCCCCCTTCTCCAAAAACTCTCATGAAGGCTCATAGTTCCACACAGCCGCC
```

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dogZO-1           TTCAAAAGCCCCTGCTTCTCCCAAGACTCTTGCAAAAGCACATAGTCGAGCACAGCCTCC
chimpanzeeZO-1    TTCAAAAACTCCCACTTCTCCAAAAACTCTTGTGAAATCGCACAGTTTGGCACAGCCTCC
                  ******* * **  **** ** ** *****    **  * ** ***    ******* **

mouseZO-1         AGAGTTTGGCAGTGGAGTTGAAACTTTCTCTGTTCACACAGATAAGCCTAAATATCAAAT
ratZO-1           TGAGTTTGACAGTGGAGTCGAGACTTTCTCTGTTCACACAGATAAGCCTAAATATCAAAT
dogZO-1           TGAGTTTGACAGTGGAGTTGAAACTTTCTCCATCCATGCAGATAAACCTAAATATCAAAT
chimpanzeeZO-1    TGAGTTTGACAGTGGAGTTGAAACTTTCTCTATCCATGCAGAGAAGCCTAAATATCAAAT
                  ******* ********* ** ********  * **  **** ** **************

mouseZO-1         GAATAATATCAGCACCATGCCTAAAGCTGTCCCTGTGAGTCCTTCAGCTGTGGAAGAAGA
ratZO-1           AAATAATATCAGCACCATGCCTAAAGCTGTTCCTGTGAGTCCTTCAGCTGTGGAAGAAGA
dogZO-1           GAACAATCTCAGCACAGTGCCTAAAGCTATTCCTGTGAGCCCGTCAGCTGTGGAAGAAGA
chimpanzeeZO-1    AAATAATATCAGCACAGTGCCTAAAGCTATTCCTGTGAGTCCTTCAGCTGTGGAAGAGGA
                  ** *** *******  ********** * ******** ** *************** **

mouseZO-1         TGAAGATGAGGATGGTCATACTGTAGTGGCTACAGCTCGTGGCATTTTTAACAGCAATGG
ratZO-1           TGAAGATGAGGATGGTCATACTGTAGTGGCTACAGCCCGCGGCATTTTTAACAGCAATGG
dogZO-1           TGAAGATGAGGATGGCCATACTGTGGTGGCCACAGCCCGAGGCGTCTTTAACAACAATGG
chimpanzeeZO-1    TGAAGATGAAGATGGTCATACTGTGGTGGCCACAGCCCGAGGCATATTTAACAGCAATGG
                  ********* ***** ******** ***** ***** ** *** * ******* ******

mouseZO-1         TGGTGTGTTGAGTTCCATAGAAACCGGTGTTAGTATAATTATCCCACAAGGAGCCATTCC
ratZO-1           CGGTGTGTTGAGTTCCATAGAAACTGGTGTTAGTATAATTATCCCACAAGGAGCCATTCC
dogZO-1           TGGGGTGTTGAGTTCCATAGAAACTGGCGTCAGTATCATCATCCCCCAAGGAGCCATTCC
chimpanzeeZO-1    GGGCGTGCTGAGTTCCATAGAAACTGGCGTTAGTATAATTATCCCTCAAGGAGCCATTCC
                  ** *** ***************** ** ** ***** ** ***** **************

mouseZO-1         TGAAGGAATTGAGCAAGAAATCTATTTCAAAGTCTGCAGAGACAATAGCATTCTCCCACC
ratZO-1           TGAAGGAATTGAGCAAGAAATCTATTTCAAAGTCTGCAGAGACAATAGCATCCTCCCACC
dogZO-1           GGAGGGAGTCGAACAGGAAATCTACTTCAAGGTCTGCCGAGACAACAGCATCCTCCCCCC
chimpanzeeZO-1    CGAAGGAGTTGAGCAGGAAATCTATTTCAAGGTCTGCCGGGACAACAGCATCCTTCCACC
                  ** *** * ** ** ******** ***** ****** * ***** ***** ** ** **

mouseZO-1         TTTAGATAAAGAGAAAGGTGAAACTCTGCTGAGCCCCCTAGTGATGTGTGGGCCCCATGG
ratZO-1           TTTAGATAAAGAGAAAGGTGAAACTCTGCTGAGCCCCCTAGTGATGTGCGGGCCCCATGG
dogZO-1           TTTAGATAAGGAGAAAGGTGAGACACTGCTGAGCCCCTTAGTGATGTGTGGGCCCCATGG
chimpanzeeZO-1    TTTAGATAAAGAGAAAGGTGAAACACTGCTGAGTCCTTTGGTGATGTGTGGTCCCCATGG
                  ********* ********** ** ******** **  * ******** ** ********

mouseZO-1         CCTCAAGTTCCTGAAGCCCGTGGAGCTACGCTTGCCACACTGTG----------------
ratZO-1           CCTCAAGTTCCTGAAGCCTGTGGAGCTACGCTTGCCACACTGTG----------------
dogZO-1           CCTCAAGTTCCTGAAGCCCGTGGAGCTGCGCTTGCCACACTGTGCGTCCATGACTCCTGA
chimpanzeeZO-1    CCTCAAGTTCCTGAAGCCTGTGGAGCTGCGCTTACCACACTGTGCGTCCATGACTCCTGA
                  ****************** ******** ***** **********

mouseZO-1         ------------------------------------------------ACCCTAAAACCTGGCA
ratZO-1           ------------------------------------------------ACCCTAAAACTTGGCA
dogZO-1           CGGTTGGTCTTTTGCTCTAAAATCATCCGACTCCTCGTCGGGTGATCCTAAAACCTGGCA
chimpanzeeZO-1    CGGTTGGTCTTTTGCTCTAAAATCATCCGACTCCTCGTCGGGTGATCCTAAAACCTGGCA
                                                   * ******** *****

mouseZO-1         AAACAAGTGTCTTCCTGGAGATCCGAATTACCTTGTTGGAGCCAACTGTGTTTCTGTCCT
ratZO-1           AAACAAGTGTCTTCCTGGAGATCCGAATTACCTTGTTGGAGCCAACTGTGTTTCTGTCCT
dogZO-1           AAACAAGTGTCTTCCTGGAGATCCAAATTACCTTGTTGGAGCAAACTGTGTTTCTGTCCT
chimpanzeeZO-1    AAACAAGTGTCTTCCCGGAGATCCAAATTATCTCGTTGGAGCAAACTGTGTTTCTGTCCT
                  *************** ******** ***** ** ******** ****************

mouseZO-1         GATTGACCACTTTTAATTCTTAGTGTATAGGAACTGGACTAAGCAATGTGAACGTGGATT
ratZO-1           GATTGACCACTTTTAATTCTTAGAGTCTAGCAGCTGGACTAAGCAGTGTGAACATGGATT
dogZO-1           GATTGACCACTTTTAATTCTTAAAATATAGGAACTTGATTAAATAATGTGAAACTGGGTT
chimpanzeeZO-1    TATTGACCACTTTTAACTCTTGAAATATAGGAACTT----AAATAATGTGAAACTGGATT
                  *************** ****    * *** * **     **  * ******  *** **

mouseZO-1         GAACTTACTAAATCTAAATGGAACCACTCTAATGAGTATTATA-TTTTCTTAGAATTTAT
ratZO-1           GAACTTACTGAA------TGGAACCACTCTAATGAGTATTCTA-TTTTCTTAGAATTTAT
dogZO-1           AAACTTACTAAATCTAAATGGAAGCACTCTATCAAGTATTATACTTTCCTTAGAATTGAT
chimpanzeeZO-1    AAACTTA----ATCTAAATGGAACCACTCTATCAAGTATTATACCTTTTTTAGAGTTGAT
                  ******    *      ***** *******   ****** **  **  ***** ** **
```

```
mouseZO-1           ACTGCAATTG-GTAGTATTAAGCATTT-GTTGGAACTGATGAAGGTTAGCGAGCATGCCC
ratZO-1             ACTGCAGTTA-GTAGTATTAAACATTT-GTTGGAACTGATAAAGGTTAGTGAGCATGCCC
dogZO-1             ACTGCAGTTC-TTAGTATTAAGCATTTTGTCTGAACAGATGAAGATTAGTGAGCATGCCC
chimpanzeeZO-1      ACTACAGTTTGTTAGTATGAAGCATTT-GTTTGAACTGATAAAGATGAGTGAGCATGCCC
                    *** ** **   ****** ** ***** **  **** *** *** * ** **********

mouseZO-1           CTGAGCCACGGTCAGAAAGCATGCTACAAGCTATGTGTTATTGAGTGA-AGAACTGTCAG
ratZO-1             CTGAACCACGATCAGAAAACATGCTACAAGCTGTGTGTTATTGAGTGG-AGAACTGTCAG
dogZO-1             CTGCACCGTGGTCAGAAAACATGCTGCAGACTGCGTGTTTGTGATGGA-AAAACCGTC-A
chimpanzeeZO-1      CTGAACCATGGTCGGAAAACATGCTACACACTGCATGTTTGTGATTGACGGGACTGTT-G
                    ***  **  * ** **** ****** **  **   ****  ***  *     ** **

mouseZO-1           GCATTGGCTAGAGGTTCAAAGATATTTTTGCTTTGTAATGATTTTTGTA-CTTTTTTATG
ratZO-1             GCATTGGCTAGAGGTTCAAAGATATTTT-GCTTTGTAATGATTTTTGTA-CTTTTTTATG
dogZO-1             GTATTGGCTGGAGGGTCAGAGATGGTTT-GCTTTGTAATGATTTTTGTA-CTTTTTTACA
chimpanzeeZO-1      GTATTGGCTAGAGGTTCAAAGATATTTT-GCTTTGT---GATTTTTGTAATTTTTTTATC
                    * ******* **** *** ****  *** *******   **********  *******

mouseZO-1           GTCACTGCTTAACTTCACATACTGATTTCCGTTAAAAATACCAGCCAGTAAATGGGGGTG
ratZO-1             GTCACTGCTTAACTTCACATACTGATTTCCGTTAAAAATACCAGCCAGTAAATGGGGGTG
dogZO-1             GTCACTGCTTA-CTTCAC----TGATTTCCGTTAAAA-TACCAGCCAGTAAATGGGG-TG
chimpanzeeZO-1      GTCACTGCTTAACTTCACATATTGATTTCCGTTAAAA-TACCAGCCAGTAAATGGGGGTG
                    *********** ******    *************** ******************* **

mouseZO-1           CATTTGAGTTCTGTTCTTTCCAAAGTACACT----CAAAGTTTATTATGGCCTTGGCCTA
ratZO-1             CATTTGAGTTTTGTTCTTTCCAAAGTACACT----CAACCTTTACTATGGCCTTGGCCTA
dogZO-1             CATTTGAGTTTTATTCTTTCCAAAGTACACTGTTTCAAACTTGATTATGGCCCTGGCTTG
chimpanzeeZO-1      CATTTGAGGTCTGTTCTTTCCAAAGTACACTGTTTCAAACTTTACTATGGCCCTGGCCTA
                    ******** * * ******************    ***  ** * ******* **** *

mouseZO-1           GCATAC----ACATTTTATTTTATTATACATGAGGTAATGTGCACACATTTTTTACAAAT
ratZO-1             GCATAC----ACATTT-ATTTTATTATGCATGAGGTAATGTGCACACATTTTTTACAAAT
dogZO-1             GCATAC----ACATTTTATTTTATTATGCATGAGGTAATATGCACACATTTAAAA---AAT
chimpanzeeZO-1      GCATACGTACACATTTTATTTTATTATGCATGAAGTAATATGCACACATTTTTTA---AAT
                    ******    ****** ********** ***** ***** ***********   *  ***

mouseZO-1           GCACCTGGAATATATAA-CCAGTATAGTGGATTTAACAGAAATGTACAGCAGGGGGA-TT
ratZO-1             GCACCTGGAATATATAA-CCAGTGTAGTGGATTTAACAGAAATGTACAGCAGGGGGA-TT
dogZO-1             ATACCTGGAGCATATAAACCAGTGTAGTAGATTTAACAGAAATGTACAGCAAGGGGAATT
chimpanzeeZO-1      GCACCTGGAATATATAA-CCAGTGTTGTGGATTTAACAGAAATGTACAGCAAGGAGA-TT
                      *******  ****** ***** * ** ********************** ** ** **

mouseZO-1           TATAACTTGGGGAGGGAGGG----------------TCAAATGAAGACAATTACTTATTG
ratZO-1             TATAACTTGGGGAGGGAGGG----------------GCAAATGAAGACAATTCCTTATTG
dogZO-1             TGTAGCTTTGGGGGGGTGGGGGGGATGGTAGGGAAGTCAAGTGAAGACAATTACTTATTG
chimpanzeeZO-1      TATAACTGGGGGAGGGTG--------------------AAGTGAAGACAGTGACTTACTG
                    * ** **  *** *** *                    ** ******** *  **** **

mouseZO-1           TATATGAAAACACATTTCTTTTAGGGAAGGACACCAAAGCATGTGAGCCCGGTTC-ATGG
ratZO-1             TATATGAAAACACATTTCTCTTAGGGAAGGACACCAAAGCATGTGAGCCCAGTTCCATGG
dogZO-1             TATATGGAAACACATTTTT-TTAGGGAAGGACACCAAAGCATGTGAGACTGGTTCTGTGG
chimpanzeeZO-1      TACATGAAAACACATTTTTCTTAGGGAAGGATACAAAAGCATGTGAGACTGGTTCCATGG
                    ** *** ********** * ********** ** ********** *  ****  ***

mouseZO-1           CCTCT---GAATCTATAAATTAAC-ATATCACCACAGACATG-TAACCAGCAGGAATGCCT
ratZO-1             CCGCT---GAATCTATAAATTAAC-ATATCACCACAGACATC-CAACCAGCAGGAATGCCT
dogZO-1             CCTCTTTGGATCTATAAATTAACCATATCACCACAGACATACTAACCAGCAGGAATGCCT
chimpanzeeZO-1      CCTCTTCACATCTCTAACTTCACCATATTACCACAGACATACTAACCAGCAGGAATGCCT
                    ** **    **** *** ** ** **** ***********   ****************

mouseZO-1           TACCCTAGTGGGTTTAATTCTTCCATCATT-TCGCTGTGTATTACTAAGTTTTTATGAGT
ratZO-1             TACCCTCATGGTTTTCATTCTTAGATCATT-TCGCTCTGTAGTACTAAGTTTTTATGAGT
dogZO-1             TACCCTCATATTTTTAATTCTTAGATCATTCTCTCTGTGTATTACTAAGTTTATATGGCT
chimpanzeeZO-1      TACCCTCATGTTCCTAATTCTTAGCTCATTCTCCCTGTGT---TACTAAGTTTTTATGGCT
                    ******  *     * ******   ***** ** ** ***  ********** ****  *

mouseZO-1           TCTGTGCAT-ATCTAGATACTGTACCATGGAAAAGACTGAGTAGATTGTGGACTTGATGG
ratZO-1             T-TGTGCGT-ACCTAGATACTGTATCATGGAAAAGACTGAGGAAATTGTGGACTTGATGG
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dogZO-1           TTTGTGCAC-ATCTAGTTACTGTATCATGAAAAAGATTGAGTAAATTGTGGATTTGGTGG
chimpanzeeZO-1    TTTGTGCATTATCTAGATACTGTATCATGACAAAGACTGAGTACATTGTGCATTTGGTGG
                  * *****   * **** ******* ****  ***** **** * ****** * *** ***

mouseZO-1         TTTCAGAAATGTGCAAATTACCTGGAAGAAAATAATGGTGTGACTTAAA-ATATTTTTTT
ratZO-1           TTTCGGAAATGTGTAAATCACCTGGAAGAAAGTAATGGTGTGACTTAAA-ATATTTTTTT
dogZO-1           TTTCAGAAATGTATAA-TCACCCAGA-GAAAATAATGGTGTGATTTGGGGATTCCCCACC
chimpanzeeZO-1    TTTCAGAAATGTGTTA-TCACCCAGAAGAAAATAGTGGTGTGATTTGGGGATATTTTTTT
                  **** *******   * * ***  ** **** ** ******** **    **

mouseZO-1         ---------GA----------------------CAGGGGGAG-----TGGCAGTCTTCTG-
ratZO-1           TT--------GA----------------------CAAGGGAGAGTGGTTGGTGGTCTTCTG-
dogZO-1           CACCACCCCCAC----------------------CAAGGGGCAG-----TGGTGGTTTTTCTG
chimpanzeeZO-1    CTTTTCTTTTCTTTTTTTTTTTTTTTTTTTGACAAGGGGCAG-----TGGTGGTTTTCTGT
                                                  ** ***         ***  ** **

mouseZO-1         TTCTTTGGGCTGTGCATCTGAGATGTTTGATGCTTTCAGGACGCATGTACATAATGCGTG
ratZO-1           TTCTTTGGGCTATGCATCTGAGATGTTTGATGTGTTCAGGACGCATGTACATAATGCGTG
dogZO-1           TTCTTTTGGCTATGCATTTGAAAATTTTGACATTTTAAGGATGCTTGTACATAATGCGTG
chimpanzeeZO-1    TCTTTCTGGCTATGCATTTGAAAATTTTGATGTTTTAAGGATGCTTGTACATAATGCGTG
                  *  **  **** ***** *** *  *****    ** **** ** **************

mouseZO-1         CATACCACTTTTGTTCTTGGTTTGTAAATTAACTTTTATAAACTTTACCTTTTT-ATACA
ratZO-1           CATACCACTTTTGTTCTTGGTTTGTAAATTAACTTTTATAAACTTTACCTTTTT-ATACA
dogZO-1           CATACCACTTTTGTTCTTGGTTTGTAAATTAACTTTTATAAACTTTACCTTTTTTATACA
chimpanzeeZO-1    CATACCACTTTTGTTCTTGGTTTGTAAATTAACTTTTATAAACTTTACCTTTTTTATACA
                  ********************************************************* *****

mouseZO-1         TAAACAGAACCAAGTTTCT-AAGGCTACCTTTGTATT-CTCTCCTGTACCTCTTGAGCCT
ratZO-1           TAAACAGAACCGAGTTTCT-AAGGCTACCTTTGTATT-CTCTCCTGTACCTCTTGAGCCT
dogZO-1           TAAACAAAACCGAGTTTCTTAAGGCTACCTTTGTATTTCTCTCCTGTACCTCTTGAGCCT
chimpanzeeZO-1    TAAACAAGACCACGTTTCTAAAGGCTACCTTTGTATT-CTCTCCTGTACCTCTTGAGCCT
                  ******  ***  ****** ***************** **********************

mouseZO-1         TGAACTTTGACCTCTGCAGCAATAAAGCAGCATTTCTA---CACATACAAGGTCATTTTT
ratZO-1           TGAACTTTGACCTCTGCAGCAATAAAGCAGCATTTCTA---CACATATAAGGTCATTTTT
dogZO-1           TGAACTTTGACCTCTGCAGCAATAAAGCAGCATTTCTATGACACATACAAGGTCATTTTT
chimpanzeeZO-1    TGAACTTTGACCTCTGCAGCAATAAAGCAGCGTTTCTATGACACATGCAAGGTCATTTTT
                  ******************************** ******   *****  ************

mouseZO-1         CT-AAGAAAAAGAATGCACAGAGTTGTTACATTTTTAAGTGCTGCATTTAAAAGATACAG
ratZO-1           TT-AAGAAAAAGAATGCACAGAGTTGTTACATTTTTAAGTGCTGCATTTAAAAGATACAG
dogZO-1           TA-AAGAAAAAGAATGCACAGAGTTGTTACATTTTTAAGTGCTGCATTTAAAAGATACAG
chimpanzeeZO-1    TTTAAGAAAAAGGATGCACAGAGTTGTTACATTTTTAAGTGCTGCATTTAAAAGATACAG
                     ********* ************************************************

mouseZO-1         TTACTC----------TAGTTTGATTAAATTCTTGCAAAGTATCCCTTCTGTAAAATTTGT
ratZO-1           TTACTC----------TAGTTTGATTAAATTCTTGCAAAGTATCCCTTCTGTAAAATTTGT
dogZO-1           TTACTCAGAATTCTCTAGTTTGATTAAATTCTTGCAAAGTATCCTGACTGTAA---TTTGT
chimpanzeeZO-1    TTACTCAGAATTCTCTAGTTTGATTAAATTCTTGCAAAGTATCCT-ACTGTAA---TTTGT
                  ******          ********************************   ******  *****

mouseZO-1         GATACAATACTGTGCCCTAAAGTGTATTTTTTTTACTAATAGACAGTTTATTATGGCACAT
ratZO-1           GATACAATGCTGTGCCCTAAAGTGTATTTTTTTTACTAATAG-----TTTATTATGGCACAT
dogZO-1           GATACCATGCTGTGCCCTAAAGTGTATTTTTTTTACTAATAGACAATTTATTATGGCACAT
chimpanzeeZO-1    GATACAATGCTGTGCCCTAAAGTGTATTTTTTTTACTAATAGACAATTTATTATGGCACAT
                  ***** ** ********************************    ***************

mouseZO-1         CAGCACGATTTCTGTTTAGATAATACACCACTACATTCTGTTAATAA-TCAGTAGGTGTG
ratZO-1           CAGCACGATTTCTGTTTAGATAATACACCACTACATTCTGTTAATAA-TCATTAGGTGTG
dogZO-1           CAGCACGATTTCTGTTTAGATAATACACCACTACATTCTGTTAATCAATCATTAGGTGTG
chimpanzeeZO-1    CAGCACGATTTCTGTTTAGATAATACACCACTACATTCTGTTAATCA-----TTAGGTGTG
                  ********************************************** *     ********

mouseZO-1         AAAGGATTTCTTTTGTGGTTATTAAAAAAAAATCTCAAATTTCTAAATCTGCAAGAATAA
ratZO-1           AAAGGATTTCTTTTGTGGTTATTAAAA-----ATCTCAAATTTCTAAATCTGCAAGAATAA
dogZO-1           ACTGAATTTCTTTTGCAGTTATTAAAAAA---TCTCAAATTTCTAAATCTGCGG-AATAA
chimpanzeeZO-1    ACTGAATTTCTTTTGCCGTTATTAAAAA----TCTCAAATTTCTAAATCTCCAA-AATAA
                  *  * **********  **********     ****************** *   *****
```

```
mouseZ0-1           AACTTTTTAAAAT----------------------------------------------------
ratZ0-1             AACTTTTTAAAATACAGT-----------------------------------------------
dogZ0-1             AACTTTTTAAAATAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA---------
chimpanzeeZ0-1      AACTTTTTAAAATAAAGTGCTGGCTTGGTCTGTTTGCCCACTGTTTTCTAGTTTCATGCA
                    **************

mouseZ0-1           ----------------------------------------------------------------
ratZ0-1             ----------------------------------------------------------------
dogZ0-1             ----------------------------------------------------------------
chimpanzeeZ0-1      GCTTTATAATCCTGTTTTAAAATCCTGCACACAAATCCCTATCACCCAGCGTCACCTACC

mouseZ0-1           ----------------------------------------------------------------
ratZ0-1             ----------------------------------------------------------------
dogZ0-1             ----------------------------------------------------------------
chimpanzeeZ0-1      ACCTCGTCGTCTGGTGTTGCATGCAGAATTTCTCCCCTTGGCCAGCATGTACAGATGGGT

mouseZ0-1           ----------------------------------------------------------------
ratZ0-1             ----------------------------------------------------------------
dogZ0-1             ----------------------------------------------------------------
chimpanzeeZ0-1      GGGCAGTGCTCATCTGAAGGGCTCAGACTGAAGTGGGGCAGAAGGACCTGGAGACAGAGT

mouseZ0-1           ----------------------------------------------------------------
ratZ0-1             ----------------------------------------------------------------
dogZ0-1             ----------------------------------------------------------------
chimpanzeeZ0-1      GGGAGAAAGCAGCAGGCCGACTTCCCCCTGTGGGTAAACACACACCCCTGCGTGGAGAAA

mouseZ0-1           --
ratZ0-1             --
dogZ0-1             --
chimpanzeeZ0-1      CA
```

query.dnd

```
(
(
mouseZ0-1:0.04818,
ratZ0-1:0.01034)
:0.06105,
dogZ0-1:0.04310,
chimpanzeeZ0-1:0.05771);
```

********** [tree] **********

```
options = -type=dna -tree -outputtree=phylip -kimura -tossgaps

 CLUSTAL W (1.83) Multiple Sequence Alignments


Sequence type explicitly set to DNA
Sequence format is Clustal
Sequence 1: mouseZ0-1          7502 bp
Sequence 2: ratZ0-1            7502 bp
Sequence 3: dogZ0-1            7502 bp
Sequence 4: chimpanzeeZ0-1     7502 bp
```

query.ph

```
(
(
mouseZ0-1:0.03100,
ratZ0-1:0.02847)
```

:0.05770,
dogZ0-1:0.04775,
chimpanzeeZ0-1:0.04326);